A STUDY ON CARDIAC ABNORMALITIES IN HIV INFECTED INDIVIDUALS

submitted to

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THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

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BONAFIDE CERTIFICATE

This is to certify that **"A STUDY ON CARDIAC ABNORMALITIES IN HIV INFECTED INDIVIDUALS"** is a bonafide work done by **Dr.V.SAKTHIVADIVEL**, post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfillment of regulations of **The Tamilnadu Dr.M.G.R.Medical University** for the award of **M.D.Degree Branch I, (General Medicine)** during the academic period from May 2006 to March 2009.

Dr. M. Dhanapal, M.D., D.M.,
Director of Medical Education – OSD
&
Dean
Kilpauk Medical College
Chennai – 10

Prof. G. Rajendran, M.D.,
Professor and Head
Department of Internal Medicine
Kilpauk Medical College
Chennai-10

Prof. A. Joseph Navaseelan, M.D.,
Professor
Department of Internal Medicine
Kilpauk Medical College
Chennai-10

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ETHICAL COMMITTEE OF
GOVERNMENT KILPAUK MEDICAL COLLEGE HOSPITAL
KILPAUK, CHENNAI-10.
Venue: Dean Chamber, Date: 3.1.2008

Chair person
Prof. Dr. M. Dhanapal, M.D, D.M.
Director of Medical Education (OSD)
&
The Dean
Govt. Kilpauk Medical College & Hospital,
Chennai - 600010.

TO WHOMSOEVER IT MAY CONCERN

Dear Sir / Madam

Sub: Internal Medicine – MD PG's Dissertation Ethical Committee – Reg.

Ref: Requisition from H.O.D. Medicine.

This is in reference to the letter dated 2.1.2008 regarding Ethical committee meeting clearance with regard to the following topics

Sl.No	Name of the Post Graduate	Dissertation Topic
1	Dr. R.Ramprasad	A study on Prevalence and Risk Factors of Diabetic Nephropathy in Newly Detected Type 2 Diabetic Patients
2	Dr. V.Sakthivadivel	A study on Cardiac abnormalities in HIV infected individuals
3	Dr. K.S.Gopakumar	A study on Subclinical Hypothyroidism in females over 50 years of age
4	Dr. T.Karthikeyan	Inflammatory profile in Acute Myocardial Infarction

5	Dr. Maliyappa Vijay Kumar	A study on Prevalence of Microalbuminuria in HIV patients not on ART and Correlation with CD4 count
6	Dr. D.Radha	High sensitivity C - reactive protein as a determinant in the outcome of Acute ischemic stroke
7	Dr. Lakshmi Thampy M.S	A Study on the prevalence of increased LV mass & Proteinuria in newly diagnosed Hypertensive patients.
8	Dr. Manu Bhasker	A study on the effect of Intravenous Metoprolol along with Thrombolysis in Acute Myocardial infarction
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10	Dr. P.Dhanalakshmi	A study On Metabolic Syndrome in Young Ischemic Stroke
11	Dr. V.Murugesan	A study on Electrocardiographic and Echocardiographic changes in Chronic Obstructive Airway Disease
12	Dr. M.Seetha	Effect of Right ventricular infarction on the immediate prognosis of Inferior wall Myocardial Infarction

We are glad to inform you that at the EC meeting held on 3.1.08 on the above topics were discussed and **Ethically approved**.

DEAN

Chair person
Prof. Dr. M. Dhanapal, M.D, D.M.
Director of Medical Education (OSD)
&
The Dean,
Govt. Kilpauk Medical College & Hospital,
Chennai - 600010.

Chairman & Members of the Ethical Committee:

Chairman

1. **Prof. Dr.M.Dhanapal M.D,D.M.,**
   Director of Medical Education(OSD).,
   & The Dean,
   Govt. Kilpauk Medical College & Hospital,
   Chennai-600 010.

2. **Dr. M.S. Ravi M.D, D.M.,**
   Prof. & HOD,
   Dept. of Cardiology

3. **Dr. Niyanthrini Sridhar MD.,**
   Prof. & HOD,
   Dept. of Micro Biology

4. **Dr. Revathi Jeyakumar M.D.,**
   Prof. & H.O.D
   Dept. of Bio-chemistry

5. **Dr. Ramachandra Bhat M.D,**
   Prof. & HOD,
   Dept. of Pharmacology

6. **Dr. Nandagopal D.V.,**
   Medical Officer,
   ART Centre

7. **Mr. A. Maria Lawrence**
   Counsellor

8. **Mr. K. Thangaraj**
   Social Worker

9. **Mrs.S.Vijayalakshmi**
   Nursing Superintendent

We confirm that no member of the study team is on the Ethics Committee and no member of the study team voted.

The trial will also follow the Ethics Guidelines for Bio-Medical Research On Human subjects issued by ICMR, New Delhi and will not involve any expense to the Government and will not be detrimental to the normal functioning of the Institution.

The study will also satisfy the revised order issued by the Government of Tamil Nadu, Health and Family Welfare Department G.O.MS.No:319, H & FW, Dept. dated 30.11.2001.

INTRODUCTION

Acquired Immuno Deficiency Syndrome was first recognized in the United States in 1981 when the U.S Center for Disease Control and prevention (CDC) reported unexplained occurrence of Pneumocystis jiroveci pneumonia in five previously healthy homosexual men. Within months, disease was recognized in injection drug users (IDUs), in recipient of blood transfusions and hemophiliacs.[1]

In 1983, Human Immuno Deficiency Virus was isolated from a patient with lymphadenopathy and in 1984 it was demonstrated clearly to be the causative agent of AIDS. [1] India's first case of AIDS was reported in 1986 from Chennai.[2]

From the beginning of the AIDS epidemic, it was recognized first at autopsy and later by non invasive techniques that HIV infection can cause cardiac abnormalities. The prevalence of cardiac disease in HIV infected individuals is not clear; the reported frequency of cardiac abnormalities depends on the population studied and the definition of cardiac abnormality.

Before the advent of Anti-retroviral therapy (ART), clinically significant cardiac disease was universal in the HIV infected population and was detected in most cases only at autopsy. However cardiac

abnormalities in AIDS patients appears to be more common than previously thought. In fact when HIV infected patients were examined by echocardiography in late 1990, cardiac abnormalities were detected more often than could be expected from clinical symptoms and physical examination. Although most conditions are clinically quiescent, some may have devastating and fatal outcomes. Pericardial effusion and Myocarditis are among the most commonly reported abnormalities though cardiomyopathy, endocarditis and coronary vasculopathy have also been reported.

It is expected that the risk of cardiac and cardiovascular disease will rise in the following years due to the cardiovascular risk profile and increased life expectancy of infected patients. Therefore diagnosis and therapy of HIV associated cardiovascular diseases should be an inherent part of current therapeutic concepts of HIV infection.

AIM OF THE STUDY

1. To study the prevalence of cardiac abnormalities in HIV infected individuals.

2. To correlate the cardiac abnormalities with CD4 cell count.

REVIEW OF LITERATURE

EPIDEMIOLOGY

GLOBAL SCENERIO OF HIV [3]

- An estimated 33 million people [30.3 – 36.1 million] were living with HIV in 2007.
- There were 2.7 million [2.2 – 3.2 million] new HIV infections and 2 million [1.8 – 2.3 million] AIDS-related deaths last year.
- The rate of new HIV infections has fallen in several countries, but globally these favourable trends are atleast partially offset by increases in new infections in other countries.
- Sub-Saharan Africa has two thirds (67%) of all people living with HIV worldwide.
- Globally, women account for half of all HIV infections—this percentage has remained stable for the past several years.
- An estimated 370000 [330000 – 410000] children (younger than 15 years) became infected with HIV in 2007.
- The total number of children living with HIV has increased from 1.6 million [1.4 – 2.1 million] in 2001 to 2 million [1.9 – 2.3 million] in 2007 - almost 90% live in sub-Saharan Africa.

INDIAN SCENERIO OF HIV [4]

- An estimated 2.47 million (2 - 3 million) peoples were living with HIV / AIDS
- HIV prevalence among people 15 to 49 years of age was 0.28% (0.23 - 0.33%)
- Prevalence of HIV in adults was 0.36%.
- Highest prevalence was found among people 30 to 34 years old – 0.64% among men and 0.45% among women.
- Prevalence was higher in urban areas than in rural areas.
- Prevalence was higher among male than female in all age groups except those 15 to 19 years of age, in which rates were very low.
- HIV prevalence was stable or declining among pregnant women in the high prevalence states of Andhra Pradesh, Karnataka and Tamil Nadu.
- HIV transmission is primarily sexual, except in northeastern India where there is high rate of spread through injection-drug use.

SCENERIO IN TAMILNADU [5]

- HIV prevalence in different population are as follows

  Antenatal clinic attendees – 0.25%

  STD clinic attendees – 8%

  Female sex workers – 4.62%

  Men having sex with men – 5.60%

  Intra venous drug users – 24.2%

District Categorization [5]

- **Category A:** More than 1% ANC prevalence in district in any of the sites in the last 3 years.

- **Category B:** Less than 1% ANC prevalence in all the sites during last 3 years with more than 5% prevalence in any HRG site (STD/FSW/MSM/IDU).

- **Category C:** Less than 1% ANC prevalence in all sites during last 3 years with less than 5% in all HRG sites, with known hot spots (Migrants, truckers, large aggregation of factory workers, tourist etc).

- **Category D:** Less than 1% ANC prevalence in all sites during last 3 years with less than 5% in all HRG sites with no known hot spots and no or poor HIV data.

- In Tamil Nadu, among 30 districts, 22 districts are in category A, 5 districts are in category B and 3 districts are in category C.

HUMAN IMMUNODEFICIENCY VIRUS [1]

The origin of HIV is unclear. The most likely scenario is that HIV was introduced into human from another primate in Sub-Saharan Africa.

ETIOLOGIC AGENT [1]

The etiologic agent of AIDS is Human Immuno Deficiency Virus (HIV) which belongs to the family of human retroviruses (Retroviridae) and the sub families of lentiviruses.There are two sub types of HIV namely HIV-1 and HIV 2.They are cytopathic viruses. HIV-2 is more similar to SIV (Simian Immuno Deficiency Virus) than HIV-1 and it is much less virulent usually not resulting in full blown AIDS, but still fatal.

MORPHOLOGY OF HIV [1]

Electron microscopy shows that the HIV is spherical enveloped virus, about 90 - 120 nm in size. The nucleocapsid has an outer icosahedral shell containing numerous external spikes formed by the two major

envelope proteins, the external gp 120 and the transmembrane gp 41. The core virus particle is composed of ribonucleoproteins.

HIV GENOME [1]

HIV-1 has the following genes. gag – encodes the proteins that form the core of virion. pol – encodes viral enzymes necessary for replication, reverse transcriptase, integrase and protease and env – encodes glycoprotein. It also contains atleast six other genes tat, rev, nef, vpr, vpu which code for proteins involved in the regulation of gene expression. The major difference between the genomes of HIV-1 and HIV-2 is the fact that HIV-2 lacks the vpu gene and has vpx gene not contained in HIV-1.

LIFE CYCLE [1]

ATTACHMENT AND ENTRY

The replication cycle of HIV begins with the high affinity binding of the gp 120 protein via a portion of its V1region near the N terminus to its receptor on the host cell surface, the CD4 molecule. It is also expressed on the surface of monocytes and dendrites / langerhans cells. Once gp 120 binds to CD4, the gp 120 undergoes a conformational change that facilitates binding to one of a group of co-receptors. The two major co-receptors are CCR5 and CXCR4.

REVERSE TRANSCRIPTION AND INTEGRATION

Following binding of the envelop protein to the CD4 molecule, the virus is “uncoated” and the viral RNA is converted into complementary DNA (C-DNA) by virion associated reverse transcriptase enzyme. The C-DNA is transported to the host cell nucleus and eventually gets incorporated into the host cell chromosomes by virus specific integrase enzyme.

TRANSCRIPTION, TRANSLATION AND REPLICATION

The integrated DNA is transcribed into messenger RNA (mRNA) which comes out into cytoplasm and viral proteins are synthesized using protein synthesizing machinery and raw material from the host cell. Some of the viral proteins are synthesized as polyproteins that are eventually cleared by the proteinase enzyme.

MATURATION AND RELEASE

Newly synthesized progeny RNA and proteins are packaged together and the newly formed virus particles are released from the infected cell by the budding process.

PROGRESSION OF ILLNESS [1]

The median time from primary HIV infection to the development of AIDS in untreated individuals is approximately 10 years. Individuals are considered to be long term survivors if they remain alive for ≥ 20 years after initial infection. It may be related to beneficial effect of ART and prophylaxis against opportunistic infections. Long term nonprogressors are those who have been infected with HIV for ≥ 10 years whose CD4 count are in the normal range and remained stable over years and who had not received ART.

The reasons being

1. Mutant nef gene of HIV
2. Heterozygosity for CCR5- Δ32 deletion
3. Heterozygosity for CCR2-64I mutation
4. Homozygosity for SDF1-3'A mutation
5. Heterozygosity for the RANTES-28G mutation

CLASSIFICATION [1]

1993 Revised classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults

Table 1

CD4+ T cell Categories	Clinical categories		
	A	B	C
	Asymptomatic, Acute (primary) HIV or PGL	Symptomatic, Not A or C Conditions	AIDS-Indicator Conditions
≥ 500 /µl	A1	B1	C1
200 - 499 /µl	A2	B2	C2
< 200/ µl	A3	B3	C3

PGL – Progressive Generalized Lymphadenopathy

HIV infected persons classified in A3, B3, C1, C2 and C3 are AIDS cases

Category A:

One or more of the following conditions in adolescents or adults (> 13 years) with documented HIV infection.

Conditions listed in categories B and C must not have occurred.

1. Asymptomatic HIV infection
2. Progressive Generalized Lymphadenopathy
3. Acute (primary) HIV infection with accompanying illness or history of acute HIV infection

Category B:

Consists of symptomatic conditions in an HIV infected adolescent or adult that are not included among conditions listed in clinical category C and that meets one of the following criteria

1. The conditions are attributed to HIV infection or are indicative of a defect in cell mediated immunity (CMI).
2. Conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection.

Examples include, but are not limited to the following.

a. Bacillary angiomatosis
b. Candidiasis, oropharyngeal (thrush)
c. Candidiasis, vulvovaginal: persistent, frequent or poorly responsive to therapy
d. Cervical dysplasia (moderate or severe) / cervical carcinoma in situ
e. Constitutional symptoms, fever or diarrhea lasting > 1 month
f. Oral hairy leukoplakia
g. Herpes zoster involving atleast 2 distinct episodes or more than one dermatome
h. Idiopathic thrombocytopenic purpura
i. Listeriosis

j. Pelvic inflammatory disease, particularly complicated by tuboovarian abscess

k. Peripheral neuropathy

Category C:

Conditions listed in AIDS surveillance case definition

a. Candidiasis of bronchi, trachea or lungs

b. Candidiasis, esophageal

c. Cervical cancer, invasive

d. Coccidioidomycosis, disseminated or extrapulmonary

e. Cryptococcosis, extrapulmonary

f. Cryptosporidiosis, chronic intestinal (> 1 month's duration)

g. Cytomegalovirus disease (other than liver, spleen or nodes)

h. Cytomegalovirus retinitis (with loss of vision)

i. Encephalopathy, HIV related

j. Herpes simplex: chronic ulcers (> 1 month's duration) or bronchitis, pneumonia or esophagitis

k. Histoplasmosis, disseminated or extra pulmonary

l. Isosporiasis, chronic intestinal (> 1 month's duration)

m. Kaposi's sarcoma

n. Lymphoma, Burkitt's (or equivalent term)

o. Lymphoma, primary of brain

p. Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary

q. Mycobacterium tuberculosis, any site (pulmonary or extrapulmonary)

r. Mycobacterium, other species or unidentified species, disseminated

s. or extrapulmonary

t. Pneumocystis jiroveci pneumonia

u. Pneumonia, recurrent

v. Progressive multifocal leukoencephalopathy

w. Salmonella septicemia, recurrent

x. Toxoplasmosis of brain

y. Wasting syndrome due to HIV

CLASSIFICATION OF HIV INFECTION (WHO CLINICAL STAGING SYSTEM) [7]

Clinical stage 1:

a. Asymptomatic

b. Persistent Generalized Lymphadenopathy

Clinical stage 2:

a. Weight loss <10% of body weight

b. Recurrent upper respiratory tract infections (e.g. bacterial sinusitis)

c. Herpes zoster

d. Angular cheilitis

e. Recurrent oral ulceration

f. Papular pruritic eruptions

g. Seborrhoeic dermatitis

h. Fungal nail infections

Clinical stage 3:

a. Weight loss > 10% of body weight

b. Unexplained chronic diarrhea > 1 month

c. Unexplained persistent fever (intermittent or constant) > 1 month

d. Persistent Oral Candidiasis (thrush)

e. Oral hairy leukoplakia

f. Pulmonary tuberculosis

g. Severe bacterial infections (e.g. pneumonia, pyomyositis)

h. Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

i. Unexplained anemia (< 8 g / dl), neutropenia (< 0.5 X 10^9 / litre) and or chronic thrombocytopenia

Clinical stage 4:

a. HIV wasting syndrome

b. Pneumocystis jiroveci pneumonia

c. Recurrent severe bacterial pneumonia

d. Toxoplasmosis of the brain

e. Chronic Cryptosporidiosis

f. Chronic Isosporiasis

g. Cryptococcosis - extrapulmonary

h. Cytomegalovirus infection (retinitis or infection of other organs)

i. HIV Encephalopathy

j. Chronic Herpes simplex infection (orolabial, genital or anorectal of > 1 month's duration or visceral at any site)

k. Disseminated endemic mycosis (Extrapulmonary Histoplasmosis, Coccidiomycosis)

l. Kaposi's sarcoma

m. Candidiasis - esophagus, trachea, bronchi or lungs

n. Disseminated non-tuberculous mycobacteria infection

o. Mycobacterium tuberculosis, extrapulmonary

p. Progressive multifocal leukoencephalopathy

q. Recurrent septicemia (including non typhoid salmonella septicemia)

r. Lymphoma (Cerebral or B cell Non-Hodgkin)

s. Invasive cervical carcinoma

t. Atypical disseminated leishmaniasis

u. Symptomatic HIV-associated nephropathy or symptomatic HIV associated cardiomyopathy

WHO CASE DEFINITION FOR AIDS SURVEILLANCE IN ADULT WHERE HIV TESTING FACILITIES NOT AVAILABLE [7]

Case definition for AIDS is fulfilled if at least two major signs and one minor sign are present

Major signs:

a. Weight loss > 10% of body weight
b. Chronic diarrhea > 1 month
c. Prolonged fever > 1 month

Minor signs:

a. Persistent cough > 1 month
b. History of herpes zoster
c. Oropharyngeal candidiasis
d. Generalized lymphadenopathy
e. Chronic progressive herpes simplex infection

WHO GUIDELINES FOR INITIATION OF ART IN ADULTS AND ADOLESCENTS [7]

Table 2

Classification of HIV associated clinical disease	WHO clinical stage	CD4 test not available or pending	CD4 test available
Asymptomatic	1	Do not treat	Treat if CD4count <200
Mild symptoms	2	Do not treat	
Advanced symptoms	3	Treat	Consider treatment if CD4 <350 and initiate ART before CD4 drops below 200
Severe / Advanced symptoms	4	Treat	Treat irrespective of CD4 count

NACO GUIDELINES FOR INITIATION OF ART IN ADULTS AND ADOLESCENTS [6]

Table 3

CD4 count (cell /mm^3)	Actions
< 200	Treat irrespective of clinical stage
200 – 350	. Offer ART for symptomatic patients . Initiate treatment before CD4 drop below 200 cells/mm^3 for asymptomatic people *
>350	Defer treatment in asymptomatic persons

* If CD4 count is between 200- 250, this should be repeated in four weeks and treatment to be considered in asymptomatic patients.

British HIV association (BHIVA) suggests initiation of ART for asymptomatic HIV infected individuals having less than 200 CD4 T cell counts.[70] International AIDS society recommends initiation of ART in asymptomatic individuals with CD4 count > 200 to 350 cells / μl and viral load 50000 - 100000 copies / ml.[71]

In a study by Ramalingam et al, conducted in 2001 have shown that mean CD4 counts in south Indian population both normal and HIV infected individuals are lower than in western population and have proposed a modified classification based on CD4 cell count for south Indians. The categories of CD4 count proposed were cell count > 300,

81 - 300, ≤ 80 cells / μL, instead of the ≥ 500, 201-499, ≤ 200 recommended by CDC(Centre for Disease Control and prevention).[72]

Kannagai et al study conducted in 2008 has shown that majority of HIV infected individuals in South India with CD4 counts of 200 - 350 cells / μL had higher viral load than that suggested by International AIDS Society.[57]

CARDIAC MANIFESTATIONS IN HIV INFECTED INDIVIDUALS

The reasons for the paucity of knowledge about the etiology of HIV associated cardiovascular diseases are

1. In the early years of AIDS epidemic, most patients died of infectious complications, before the manifestations of cardiovascular complications.
2. Because cardiomyocytes do not have CD4 receptors, the heart was thought to be unaffected by HIV infection.
3. Presence of cardiovascular risk factors like poor nutrition, alcohol and drugs that can lead on to cardiac disease in HIV infected individuals.
4. Cardiac disease remains relatively asymptomatic in early stages of HIV infection.

5. Heart disease can be overlooked in HIV-positive patients, because symptoms of breathlessness, fatigue and poor exercise intolerance are frequently ascribed to other conditions associated with HIV infection.

Some form of heart disease is demonstrable at autopsy in approximately 40% of cases and by echocardiography in 25% of patients with AIDS. Many of these lesions are mild, and HIV related heart disease probably causes symptoms in less than 10% and death in less than 2% of all patients with HIV infection.[8]

At the beginning of the epidemic, heart muscle disease was the dominant cardiac complication of HIV infection in developed world, and tuberculous pericarditis in Africa. The advent of HAART (highly active anti-retroviral therapy) has changed the pattern of disease in developed countries where premature coronary artery disease and other manifestations of atherosclerosis are now the most common cardiovascular disorder. This is partly caused by HAART-induced metabolic problems, particularly insulin resistance and hyperlipidemia, but also reflects a high prevalence of conventional risk factors such as smoking.[8]

Cardiac problems associated with advanced immunodeficiency, such as heart muscle disease, pericardial effusion and pulmonary hypertension continue to predominate in resource-poor countries where less than 5% of patients are able to access anti-retroviral drugs.[8]

CARDIAC MANIFESTATIONS OF HIV/AIDS [8]

Table 4

Pericardial effusion	. Idiopathic . Infections (viral, bacterial and fungal) . Neoplastic (Kaposi's sarcoma and Non Hodgkins Lymphoma)
Heart muscle disease	. Myocarditis (idiopathic / lymphocytic, infections, toxins) . Dilated cardiomyopathy & Left Ventricular dysfunction
Endocarditis	. Marantic (nonbacterial thrombotic endocarditis) . Infective
Tumors	. Kaposi's sarcoma . Lymphoma
Right ventricular dysfunction & Pulmonary hypertension	. Primary . Secondary (recurrent chest infections, thromboembolism)
Premature atherosclerosis and Coronary artery disease	. Protease inhibitors, chronic inflammation,
Autonomic dysfunction	. CNS disease, drugs, prolonged immunodeficiency, malnutrition
Arrythmias	. Drugs, autonomic dysfunction, acidosis, electrolyte abnormalities
Vasculitis	. Antibiotics and antivirals
Adverse drug effects	. Hyperlipidemia . Proarrythmia

CARDIOVASCULAR ASSESMENT OF THE HIV/AIDS PATIENT

Heart disease can be overlooked in HIV-positive patients, because symptoms of breathlessness, fatigue and poor exercise intolerance are frequently ascribed to other conditions associated with HIV infection.[9] Echocardiographic assessment of HIV patients is extremely useful and can be used to identify those cardiac conditions that can be associated with poor outcome: pericardial effusion,[10] left ventricular (LV) systolic dysfunction / heart muscle disease,[9] intracardiac masses.[11]

INDICATIONS FOR ECHOCARDIOGRAPHIC ASSESSMENT OF HIV POSITIVE PATIENTS [8]

1) Possible baseline assessment at the time of diagnosis of HIV infection

2) Base line assessment and 1 - 2 yearly monitoring of patient with

i) Clinical manifestations of possible cardiac involvement

- Unexplained dyspnea / hypoxia
- Third heart sound, inappropriate tachycardia
- Raised jugular venous pressure
- Peripheral edema / right heart failure
- Radiographic evidence of cardiomegaly

ii) viral coinfection

- Cytomegalovirus

- Epstein-Barr virus
- Coxsackie virus
- Adeno virus

iii) History of preexisting cardiac disease

- Left ventricular systolic dysfunction (any cause)
- Valvular heart disease
- Suspicion of infective endocarditis in intravenous drug users

iv) High-risk HIV patients with:

- Wasting
- Encephalopathy
- CD4 count < 100 cells / mm^3 or AIDS
- Potentially cardiotoxic medications
- Multiple hospitalizations

3) Possible 1-2 yearly monitoring of asymptomatic HIV positive patients

4) Frequent assessment of HIV positive patients with cardiovascular involvement (as guided by cardiologist)

HIV/AIDS AND THE PERICARDIUM

Pericardial effusion and pericarditis are the most common abnormalities found in early HIV/AIDS autopsy studies. Effusions are generally small and asymptomatic.

Pericardial effusion may be related to an opportunistic infection, metabolic abnormality or malignancy, but most often a clear etiology is not found. The effusion is often part of a generalized serous effusive process also involving pleural and peritoneal surfaces. This capillary leak syndrome may be related to enhanced cytokine production in the later stages of HIV disease. Other causes can include uremia from HIV-associated nephropathy.[12] Effusion markedly increases the mortality.

Screening echocardiography is recommended for HIV-infected individuals regardless of the stage of the disease.[13] Patients should undergo pericardiocentesis if they have pericardial effusion and clinical signs (elevated jugular venous pressure, dyspnea, hypotension, persistent tachycardia, pulsus paradoxus) or Echocardiographic signs of tamponade (Continuous Wave Doppler evidence of respiratory variation in valvular flow, septal bounce, right ventricular collapse, a large effusion).[14]

Patients with pericardial effusion without tamponade should be evaluated for treatable opportunistic infections, such as tuberculosis and for malignancy. Repeated echocardiography is recommended after one month or sooner if clinical symptoms direct.[14]

HIV/AIDS AND THE MYOCARDIUM

MYOCARDITIS

Numerous pathologic studies have confirmed the presence of varying histologic patterns of lymphocytic myocarditis in HIV patients.[15] As such, estimates of the prevalence of myocarditis in HIV/AIDS varies from 53% [16] in the pre-HAART era to much lower levels today in the developed world.[17]

There are several hypotheses regarding the etiology of myocarditis in AIDS including:

1) Primary HIV myocarditis
2) Secondary HIV myocarditis
3) Opportunistic infections
4) Autoimmunity

1) Primary HIV Infection of the Myocardium

HIV neither has been universally accepted nor unambiguously proven causative agent of myocarditis in AIDS.

Although HIV can clearly infect monocytes/macrophages and myocardial interstitial cells, evidence proving that HIV can infect human cardiac myocytes which do not possess CD4 receptor is less clear.[8]

HIV gene sequences have been detected by PCR in microdissected endomyocardial biopsies from HIV-positive patients some of whom had cardiac symptoms.[18] HIV has also been shown gain entry into human fetal cardiac myocyte by ingestion through a specific crystallizable fragment (of immunoglobulin) (Fc) receptor, and it remains possible that this or other, unidentified mechanisms can promote HIV entry into the myocyte and facilitate a primary HIV myocarditis.[19]

2) Secondary HIV Myocarditis

Interstitial lymphocytes and macrophages can form contact with myocytes causing focal loss of basement membrane through a local reaction.[20] Proteolytic enzymes released through HIV replication in the interstitium could also damage myocytes.[21] The HIV envelope glycoprotein group 120 can induce tumor necrosis factor-α (TNF-α) expression from macrophages and has been shown to enhance IL-1induced nitric oxide production in neonatal rat cardiac myocytes.[22] Cytokine IL-6 which has some effect on immune response and viral replication in murine myocarditis, has been found in excess in small number of HIV-positive patients with biopsy proven myocarditis.[23]

3) Myocardial Opportunistic Infections in HIV/AIDS

Autopsy has confirmed a variety of opportunistic infections of the myocardium in patients with AIDS. Infectious agents included Toxoplasma gondii, Cryptococcus, cytomegalovirus, Candida, Pneumocystis jiroveci, Microsporidium, Histoplama capsulatum, Atypical mycobacteria and Aspergillus organisms involving the myocardium.[8]

4) Autoimmunity

Many autoimmune processes have been described in association with HIV/AIDS infection. HIV infection can itself trigger autoimmune phenomenon in susceptible patients.[24] The presence of auto antibodies along with hypergammaglobulinemia and elevated circulating immune complexes suggests that yet unidentified autoimmune process can take place in HIV positive patients.[25]

The symptoms of myocarditis are protean and include fatigue, dyspnea and pleuritic chest pain. The signs are unexplained tachycardia, third heart sound or a friction rub. ECG may show nonspecific conduction defects, repolarization abnormalities and ST-T wave changes, although these are not invariable. Chest radiograph can be normal or suggest cardiac enlargement with pulmonary congestion. Echocardiography is usually non diagnostic but can show hyperdynamic LV function in HIV-positive children or occasionally LV dyskinesia in adult AIDS patients.[8]

DILATED CARDIOMYOPATHY AND LEFT VENTRICULAR DYSFUNCTION IN HIV/AIDS

The prevalence of heart muscle disease appears to be approximately 4.4% for dilated cardiomyopathy and 6.4% for isolated LV dysfunction and the condition can cause symptoms in up to 5.5% of HIV/AIDS patients.[9] The presence of dilated cardiomyopathy is ominous and associated with poor survival compared to patients with structurally normal hearts. This poor outlook remained true even after correcting CD4 counts.

Mechanisms of Cardiomyopathy in HIV/AIDS

The mechanisms for the development of LV dysfunction, cardiomyopathy in AIDS remain unclear. In addition to the role of HIV, lymphocytic myocarditis, cytokines and autoimmune responses, the contributions of illicit and prescribed medications, nutritional deficiencies and other factors also appears to be pathogenetically or pathophysiologically important.[15]

Drug Induced Heart Muscle Disease

Zidovudine and other Nucleoside Reverse Transcriptase Inhibitors (NRTIs) can be implicated in the development of some cases of heart muscle disease. In addition to inhibiting HIV reverse transcriptase, the

drug causes a dose dependent reversible skeletal myopathy by altering mitochondrial DNA replication.[26] Foscarnet in CMV infection associated with reversible congestive cardiac failure as has doxorubicin and interferon-α therapy in Kaposi's sarcoma.[8]

The effect of recreational drugs like cocaine use has been associated with myocarditis and a possibly reversible dilated cardiomyopathy in non-AIDS patients should be considered in the HIV population.[27]

Nutritional Deficiencies and Cardiac Dysfunction in HIV/AIDS

HIV/AIDS patients with evidence LV systolic dysfunction should be assessed for micro nutrient deficiency, which is common in HIV infected individuals. Abnormally low levels of selenium and antioxidants have been demonstrated and oxidative stress can be an important mechanism for cellular damage in AIDS.[28] Selenium deficiency is implicated in the pathogenesis of Keshan disease, a specific form of dilated cardiomyopathy in China, which can respond to dietary supplementation. In the same way, decreased selenium content has been demonstrated in the hearts of AIDS patients.[29]

L- Carnitine deficiency has also been described in HIV patients, possibly in association with cardiac symptoms and in whom supplementation can be advantageous. Experimentally, Carnitine

administration reversed myopathic changes induced by Zidovudine (AZT) in vitro, but the clinical effects have yet to be established.[30]

The echocardiographic features of dilated cardiomyopathy is global LV systolic dysfunction with the consistent feature of reduced ejection fraction.[31] LV dilatation can result in mitral valve distortion and lead to regurgitation. In AIDS patients, mitral regurgitation has also been described with infective endocarditis.[32] Abnormalities of mitral flow, specifically reduced early mitral peak velocity (E) and other indices of diastolic dysfunction have been noted early in the course of HIV/AIDS with normal ejection fraction and in association with LV systolic dysfunction.[33]

No randomized trials have been reported regarding the effectiveness of current heart failure therapies in people with HIV/AIDS.[9] Common agents such as diuretics, aldosterone antagonists, and digoxin can improve well being. Angiotensin inhibitors can be poorly tolerated, possibly because many patients already have low systemic vascular resistance.[34] Etarnacept, pentoxifylline have been used in severe heart failure with some success.[35,36]

Intravenous immunoglobulin therapy has been used successfully in children with symptomatic HIV heart muscle disease and can be protective

against the development of LV dysfunction in that group.[37] The use of cardiac resynchronization therapy has not been described in HIV population, although case reports of successful use of LV assist devices [38] and orthotopic heart transplant[39] exist, although these are uncommon.

NONBACTERIAL THROMBOTIC ENDOCARDITIS

Marantic or nonbacterial thrombotic endocarditis (NBTE) is a condition in which friable clumps of platelets and red cells adhere to the cardiac valves. Unlike bacterial endocarditis these lesions are not infective and show no evidence of an inflammatory reaction.

The pathogenesis is not fully understood, but hypercoagulability, immune complex deposition, or specific vitamin deficiency can be important in conjunction with endothelial damage from intravenous catheters or injected particulate matters. Any heart valve can be affected and frequently multiple lesions are found on different levels.[40]

Treatment should focus on reducing the underlying disease causing coagulation abnormalities, valvular endothelial damage or both. An anticoagulation risk benefit assessment must be made on individual basis.[14]

INFECTIVE ENDOCARDITIS

The immunological abnormalities associated with HIV render patients susceptible to bacterial infections. The clinical presentation is

same for both HIV positive and negative patients but runs a more fulminant course in later stages of AIDS.[41] The most common valve involved is the tricuspid valve as with infective endocarditis in HIV negative intravenous drug users. Most frequently isolated organisms include staphylococcus aureus, salmonella species, streptococcus viridans but fungal endocarditis can occur in end-stage AIDS.[14] Antimicrobial treatment may have to be widened. Operative indications include hemodynamic instability, failure to sterilize blood cultures after appropriate intravenous antibiotics and severe valvular destruction in patients with reasonable life expectancy after recovery from surgery.[14]

CARDIAC TUMORS IN HIV/AIDS

Kaposi's sarcoma (KS) is the most common AIDS related neoplasia; there is often widespread and potentially fatal visceral involvement in HIV- positive individuals. The prevalence of cardiac Kaposi's sarcoma appears to have decreased significantly since early reports.[34]

It's not usually associated with symptoms of cardiac dysfunction; but cases of fatal tamponade associated with the tumor have been reported, and heart failure without ventricular dilatation can occur in cases with extensive myocardial infarction.[8] Kaposi's sarcoma can be treated with daunorubicin**,** doxorubicin or related anthracyclines. Liposomal

encapsulated daunorubicin has an improved pharmacological profile and can therefore be preferred in patients with Kaposi's sarcoma and AIDS.[42]

Non Hodgkin's Lymphoma (NHL) can involve the pericardium or myocardium. Cardiac lymphoma commonly gives rise to clinical symptoms of tamponade, heart failure, and conduction abnormalities or superior vena cava syndrome. Systemic chemotherapy with or without concomitant radiation or surgery has been beneficial in some patients, but overall the prognosis is poor.[8]

RIGHT VENTRICULAR DYSFUNCTION

Isolated right ventricular dysfunction without pulmonary hypertension is of unknown significance and can be related to changes in pulmonary circulation. Therefore bronchopulmonary infections should be treated aggressively and intravenous drug use, which can result in micro vascular pulmonary emboli should be discouraged.[8]

PULMONARY HYPERTENSION

Primary pulmonary hypertension is estimated to occur in 0.5% of hospitalized AIDS patients.[43,44] Although pulmonary hypertension can be related to the action of viral proteins [45,46] or the action of cytokines on the endothelial cell, characteristic pulmonary arteriopathy is found in HIV-related pulmonary hypertension. Right heart catheterization can be

worthwhile to determine if pulmonary hypertension can be reversed and has been used in HIV patients.[47] HAART itself can be beneficial in terms of outcome in pulmonary hypertension [48] but agents like bosentan, epoprostenol,[47] treprostinil [49] or sildenafil can improve feeling of well being without altering prognosis.

ACCELERATED ATHEROSCLEROSIS

Accelerated atherosclerosis has been observed in young HIV-infected adults and children without traditional coronary risk factors.[50,51] Protease inhibitor therapy markedly alters lipid metabolism and can be associated with premature atherosclerotic disease. Chronic inflammatory states have also been associated with atherosclerotic disease. Atherosclerotic disease is believed to have multi factorial causes and is prone to plaque rupture, possibly related to the host environment.[52] Lipodystrophy should be recognized and treated because of an elevated 10 year cardiovascular risk.[44,51] Risk stratification based on traditional risk factors plus diet, alcohol intake, physical exercise, hypertriglyceridemia, cocaine use, heroin use, thyroid disease, renal disease and hypogonadism should be considered for long term cardiac preventive care.[13,51,53]

VASCULITIS

Most types of vasculitis have been reported in HIV-infected patients. Vasculitis should be suspected in patients with fever of unknown origin, unexplained multi system disease, arthritis or myositis, glomerulonephritis, peripheral neuropathy (especially mononeuritis multiplex) and unexplained gastrointestinal, cardiac or central nervous system ischemia. Immunomodulatory therapy, chiefly with systemic corticosteroid therapy has been successful.[14]

AUTONOMIC DYSFUNCTION

Early signs of autonomic dysfunction include syncope and presyncope, diminished sweating, diarrhea, bladder dysfunction and impotence. Patients with HIV - associated nervous system disease have the greatest abnormalities in autonomic function.[54]

DISORDERS OF RHYTHM

Sudden death and rhythm abnormalities are common in HIV infection and account for 20% of cardiac related death in this group of patients. These can be secondary to other cardiac pathology or be a consequence of some forms of treatment like pentamidine induced torsade de pointes ventricular tachycardia.[8] HIV infection itself is associated with

QT prolongation and torsades de pointes ventricular tachycardia. The incidence increases with progression to AIDS.[55]

Hepatitis C is independently associated with increased QT duration and co infection with HIV nearly doubles the risk.[56] Concomitant electrolyte abnormalities can be important in development of cardiac arrhythmia. ECG abnormalities and rhythm disturbances are not uncommon findings in HIV positive patients with myocarditis or heart muscle disease and ectopic beats, ventricular tachycardia, and sudden death have also been reported.[8]

MATERIALS AND METHODS

Place of study – Department of Medicine, Kilpauk Medical College and Hospital

Collaborating Department – ART Centre, Department of Cardiology, Kilpauk Medical College and Hospital

Duration of the study – January 2008 to June 2008

Type of study – Cross sectional study

STUDY POPULATION

A total of 200 patients were randomly chosen at the start of the study. Fifty patients were excluded from study because of exclusion criteria. Remaining 150 patients were divided into two groups depending on the CD4 count. Group I included patients with CD4 count $\leq$ 350 cells / mm^3. Group II included patients with CD4 count > 350 cells / mm^3. Because majority of the individuals in South Indian populations with CD4 counts of 200 - 350 cells / mm^3 have high viral road than North Indian and Western counter parts,[57] an attempt was made to find out the cardiac abnormalities with CD4 count of 350 cells / mm^3 as a dividing line instead of CD4 count of 200 cells / mm^3.

INCLUSION CRITERIA

1. Patients who have been diagnosed as HIV positive by ELISA method

EXCLUSION CRITERIA

1. Age less than 18 years and more than 55 years

2. Treatment with anti-retroviral drugs or any cardiotoxic drugs

3. Diabetes

4. Hypertension

5. Previous congenital or acquired heart disease

6. Neoplastic diseases

7. Family history of cardiovascular diseases

8. Patients having lipid profile abnormalities

RISK FACTOR ASSESSMENT QUESTIONNAIRE

All HIV infected individuals who were included in this study were subjected to a questionnaire to assess the risks of acquiring HIV, risk factors for cardiac disease and symptomatology of cardiac illness.

To assess the risk of acquiring HIV, history regarding their sexual exposures, use of intravenous drugs and history of blood transfusion were

asked. The individual's occupation, marital status, extramarital and premarital sexual exposures, history of past and present sexually transmitted infections were also noted.

To assess the risk factors for cardiac disease, questions regarding duration and amount of smoking and alcohol consumption were asked.

To assess the symptoms of cardiac disease questions regarding presence of chest pain, breathlessness, palpitation, pedal edema and fatigue were asked. Duration of each symptom was also noted.

CLINICAL EXAMINATION

All patients were meticulously examined for the presence of anemia, cyanosis, clubbing, pedal edema, dyspnea, jaundice, generalized lymphadenopathy and skin and mucous membrane lesions. Respiratory rate, pulse rate, jugular venous pressure, blood pressure (both in supine and erect posture) were also recorded.

A thorough clinical examination of the cardiovascular system, respiratory system, abdomen and central nervous system was done.

LABORATORY INVESTIGATIONS

All of them were subjected to the following investigations.

Complete blood count, blood urea and sugar, serum creatinine and electrolytes, liver function tests (serum bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase) and Serum lipid profile were done for all patients.

A standard 12 lead resting electrocardiogram was taken for all individuals in this study.

CD4 Count Assay

The standard method for enumerating CD4 T cells uses a flow cytometer. Computer calculates the number of CD4 T cells by analyzing the size of the cell and which of the antibodies it has been tagged with. The overall process is called Fluorescence Activated Cell Sorting (FACS).

IMAGING

Chest Skiagram

An erect X-ray of the chest on deep inspiration in the postero-anterior view was taken for all patients.

Echocardiography

Two dimensional Echocardiography was done for all patients included in this study in Department of Cardiology, Kilpauk Medical College Hospital, Chennai.

Statistical analysis

Statistical analysis was done by using windows SPSS software (version 11.5). Chi square test was applied for significance. "P" value less than 0.05 was considered as significant.

REFERENCE VALUE USED IN THIS STUDY

BMI (WHO criteria for Asian population) [58]

Body Mass Index = Weight (kg) / Height in meter ^{2}

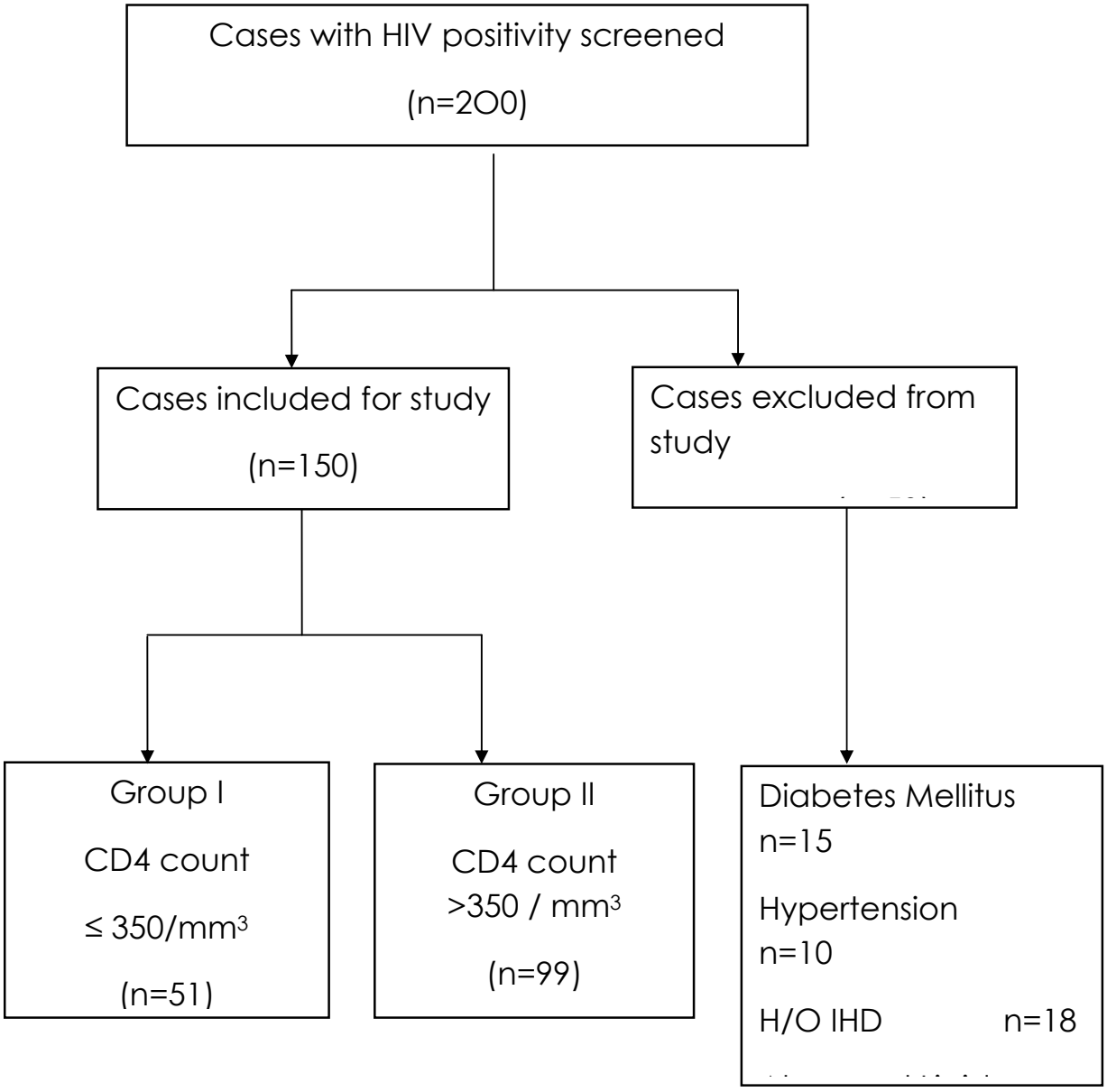
Values 18.5 - 22.9 kg / m^2 was taken as normal weight

< 18.5 kg / m^2 was taken as underweight

23- 29.9 kg / m^2 was taken as overweight

≥ 30 kg / m^2 was taken as obesity

CASE SCREENING - FLOW CHART



n - Number

RESULTS

1. A total of 150 HIV seropositive patients were studied. They were divided into two groups.

2. Group I included 51 HIV seropositive patients with CD4 cell count ≤ 350 cells / mm^3 (n=51).

3. Group II included 99 HIV seropositive patients, with CD4 count > 350 cells / mm^3 (n=99).

4. Mean CD4 count of study population was 473.34 ± 223.20 cells / mm^3 (Group I - 261.08 ± 83.75 cells / mm^3 ; Group II was 582.69 ± 191.24 cells / mm^3).

5. Out of 150 patients, 62 (41.3%) were males (Group I - 30; Group II - 32) and 88 (58.7%) were females (Group I – 21; Group II – 67).

6. Mean age of study group was 30.87 ± 6.11 years (Group I - 31.43 ± 6.23 years; Group II - 30.58 ± 6.06 years).

7. House wives and unskilled labourers constituted the majority of the study group about 35% and 34.9% respectively.

8. Heterosexual route was the most common mode of transmission of HIV infection about 95.3%.

9. Mean duration of HIV infection was 3.18 years (Group I – 2.95 years; Group II – 3.3 years)

10. Smokers and alcoholics constituted 7.3% (11 patients) and 8% (12 patients) of the study population respectively.

11. Mean BMI was 20.40 ± 3.89 kg / m^2 (Group I and Group II were 19.85 ± 4.01 kg / m^2 and 20.68 ± 3.82 kg / m^2 respectively).

12. Most patients were asymptomatic. Cardiac symptoms were found in 10 (6.7%) patients (Group I - 9; Group II – 1).

13. Twenty three patients (15.3%) (Group I – 15; Group II - 8) were found to have opportunistic infections. Oral candidiasis was the most common opportunistic infection followed by Tuberculosis and Herpes zoster.

14. Cardiac abnormalities either in the form of Electrocardiography or Echocardiography abnormality was found in 25 (16.7%) patients (Group I – 16; Group II – 9).

15. Twenty two (14.7%) patients had Electrocardiographic abnormalities (Group I – 14; Group II – 8).

16. Echocardiography abnormality was seen in 16 (10.7%) patients (Group I – 13; Group II – 3). Pericardial effusion was the most common abnormality.

17. Significant correlation was found between CD4 count, duration of HIV infection, cardiac symptoms and opportunistic infections with cardiac abnormalities.

18. There was no significant correlation between age, sex, BMI, smoking and alcohol with cardiac abnormalities.

CD4 GROUP

Table 5

CD4 GROUP	NUMBER OF PATIENTS	CD4 COUNT cells / mm^3	MEAN CD4 COUNT cells / mm^3
I	51	≤ 350	261.08 ± 83.75
II	99	> 350	582.69 ± 191.24
TOTAL	150		473.34 ± 223.20

Mean CD4 count in study population was 473.34 ± 223.20cells / mm^3.

Mean CD4 count in Group I was 261.08 ± 83.75 cells / mm^3.

Mean CD4 count in Group II was 582.9 ± 19.24 cells / mm^3.

CARDIAC ABNORMALITIES

Table 6

CARDIAC ABNORMALITIES	NUMBER OF PATIENTS	PERCENTAGE
PRESENT	25	16.70%
ABSENT	125	83.30%
TOTAL	150	100%

Prevalence of cardiac abnormalities either in the form of electrocardiography or echocardiography abnormality was 16.7%.

CD4 GROUP AND CARDIAC ABNORMALITIES

Table 7

CD4 GROUP	CARDIAC ABNORMALITIES		TOTAL
	PRESENT	ABSENT	
I	16	35	51
II	9	90	99
TOTAL	25	125	150

P value was 0.001 statistically significant.

There was a statistically significant difference observed between CD4 group and cardiac abnormalities. Prevalence of cardiac abnormalities increased with decline in CD4 count ($P < 0.05$).

AGE DISTRIBUTION IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 8

CD4 GROUP	MEAN AGE (Years)
I	31.43 ± 6.23
II	30.58 ± 6.06
TOTAL	30.87 ± 6.11

Mean age in study population was 30.87 ± 6.11 years.

Mean age in Group I was 31.43 ± 6.23 years.

Mean age in group II was 30.58 ± 6.06 years.

Table 9

AGE IN YEARS	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
20-25	3 (5.9%)	6 (11.8%)	9 (17.6%)	3 (3.1%)	14 (14.1%)	17 (17.2%)
26-30	4 (7.8%)	13 (25.5%)	17 (33.3%)	4 (4.1%)	38 (38.4%)	42 (42.4%)
31-35	6 (11.8%)	8 (15.7%)	14 (27.5%)	1 (1%)	21 (21.2%)	22 (22%)
36-40	1 (2%)	7 (13.7%)	8 (15.7%)	1 (1%)	13 (13.1%)	14 (14%)
≥ 41	2 (3.9%)	1 (2%)	3 (5.9%)	0 (0%)	4 (4%)	4 (4%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.352 statistically not significant.

P value for Group II was 0.639 statistically not significant.

There was no statistically significant difference noted between age and cardiac abnormalities in both the groups (P > 0.05).

SEX DISTRIBUTION IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 10

SEX	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
MALE	9 (17.6%)	21 (41.2%)	30 (58.8%)	5 (5.1%)	27 (27.3%)	32 (32.3%)
FEMALE	7 (13.7%)	14 (27.5%)	21 (41.2%)	4 (4%)	63 (63.6%)	67 (67.7%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.801 statistically not significant.

P value for Group II was 0.118 statistically not significant.

There was no statistically significant difference noted between sex and cardiac abnormalities in both the groups (P > 0.05).

OCCUPATION

Table 11

OCCUPATION	TOTAL
1. Unskilled labourer	52 (34.7%)
2. Skilled labourer	10 (6.67%)
3. Lorry driver	27 (18%)
4. Commercial sex worker	2 (1.3%)
5. Office worker	4 (2.7%)
6. House wife	53 (35.3%)
7. Landlord/ Business man	2 (1.3%)

ROUTE OF TRANSMISSION

Table 12

ROUTE OF TRANSMISSION	TOTAL
1. Heterosexual	143 (95.3%)
2. Homosexual	1 (0.7%)
3. Bisexual	1 (0.7%)
4. IV drug users	2 (1.3%)
5. Blood transfusion	2 (1.3%)
6. Unknown	1 (0.7%)

BMI IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 13

CD4 GROUP	MEAN BMI (kg / m^2)
I	19.85 ± 4.01
II	20.68 ± 3.82
TOTAL	20.40 ± 3.89

Mean BMI in study population was 20.40 ± 3.89 (kg / m^2).

Mean BMI in Group I was 19.85 ± 4.01 (kg / m^2).

Mean BMI in group II was 20.68 ± 3.82 (kg / m^2).

Table 14

BMI	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
UNDER WEIGHT	7 (13.7%)	14 (27.5%)	21 (41.2%)	1 (1%)	28 (28.3%)	29 (29.3%)
NORMAL	7 (13.7%)	13 (25.5%)	20 (39.2%)	6 (6.1%)	42 (42.4%)	48 (48.5%)
OVER WEIGHT	2 (3.9%)	8 (15.7%)	10 (19.6%)	1 (1%)	18 (18.2%)	19 (19.2%)
OBESE	0 (0%)	0 (0%)	0 (0%)	1 (1%)	2 (2%)	3 (3%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.684 statistically not significant.

P value for Group II was 0.234 statistically not significant.

There was statistically no significant difference noted between BMI and cardiac abnormalities in both the Groups (P > 0.05).

WHO STAGING IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 15

WHO STAGING	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
STAGE 1	3 (5.9%)	13 (25.5%)	16 (31.4%)	4 (4%)	55 (55.6%)	59 (59.6%)
STAGE 2	3 (5.9%)	12 (23.5%)	15 (29.4%)	2 (2%)	25 (25.3%)	27 (27.3%)
STAGE 3	7 (13.7%)	10 (19.6%)	17 (33.3%)	3 (3%)	10 (10.1%)	13 (13.1%)
STAGE 4	3 (5.9%)	0 (0%)	3 (5.9%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.024 statistically significant.

P value for Group II was 0.169 statistically not significant.

There was a statistically significant difference noted between WHO staging and cardiac abnormalities in Group I (P < 0.05) in contrast to Group II (P > 0.05) which was insignificant.

DURATION OF HIV INFECTION IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 16

CD4 GROUP	MEAN DURATION (Years)
I	2.95
II	3.3
TOTAL	3.18

Mean duration of HIV infection in study population was 3.18 years.

Mean duration of HIV infection in Group I was 2.95 years.

Mean duration of HIV infection in Group II was 3.3 years.

Table 17

DURATION OF HIV	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
< 1 year	3 (5.9%)	7 (13.7%)	10 (19.%)	1 (1%)	8 (8.1%)	9 (9.1%)
1- 3 years	4 (7.8%)	26 (51%)	30 (58.8%)	1 (1%)	68 (68.7%)	69 (9.7%)
>3 years	9 (17.6%)	2 (3.9%)	11 (21.6%)	7 (7.1%)	14 (14.1%)	21 (21.2%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.0001 statistically significant.

P value for Group II was 0.000 statistically significant.

There was a statistically significant increase in cardiac abnormalities observed as the duration of HIV infection increases in both the groups ($P < 0.05$).

SMOKING IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 18

SMOKING	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	2 (3.9%)	2 (3.9%)	4 (7.8%)	0 (0%)	7 (7.1%)	7 (7.1%)
ABSENT	14 (27.5%)	33 (64.7%)	47 (92.2%)	9 (9.1%)	83 (83.8%)	92 (92.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.403 statistically not significant.

P value for Group II was 0.385 statistically not significant.

There was no statistically significant difference noted between smoking and cardiac abnormalities in both the groups ($P > 0.05$).

ALCOHOL IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 19

ALCOHOL	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	3 (5.9%)	4 (7.8%)	7 (13.7%)	0 (0%)	5 (5.1%)	5 (5.1%)
ABSENT	13 (25.5%)	31 (60.8%)	44 (86.3%)	9 (9.1%)	85 (85.9%)	94 (94.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.481 statistically not significant.

P value for Group II was 0.468 statistically not significant.

There was no statistically significant difference noted between alcohol and cardiac abnormalities in both the groups (P > 0.05).

CARDIAC SYMPTOMS IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 20

SYMPTOMS	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	9 (17.6%)	0 (0%)	9 (17.6%)	1 (1%)	0 (0%)	1 (1%)
ABSENT	7 (13.7%)	35 (68.6%)	42 (82.4%)	8 (8.1%)	90 (90.9%)	98 (99%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	99 (90.9%)	99 (100%)

P value for Group I was 0.000 statistically significant.

P value for Group II was 0.001 statistically significant.

A statistically significant correlation was found between cardiac symptoms and cardiac abnormalities in both the groups ($P < 0.05$).

OPPORTUNISTIC INFECTIONS

Table 21

OPPORTUNISTIC INFECTIONS	TOTAL
Absent	127 (84.7%)
Oral Candidiasis	13 (8.7%)
Tuberculosis	6 (4%)
Herpes zoster	4 (2.7%)
Total	150 (100%)

OPPORTUNISTIC INFECTIONS IN RELATION TO CARDIAC ABNORMALITIES AND CD4 COUNT

Table 22

OPPORTUNISTIC INFECTIONS	CD4 GROUP I			CD4 GROUP II		
	CARDIAC ABNORMALITIES			CARDIAC ABNORMALITIES		
	PRESENT	ABSENT	TOTAL	PRESENT	ABSENT	TOTAL
PRESENT	8 (15.7%)	7 (13.7%)	15 (29.4%)	2 (2%)	6 (6.1%)	8 (8.1%)
ABSENT	8 (15.7%)	28 (54.9%)	36 (70.6%)	7 (7.1%)	84 (84.8%)	91 (91.9%)
TOTAL	16 (31.4%)	35 (68.6%)	51 (100%)	9 (9.1%)	90 (90.9%)	99 (100%)

P value for Group I was 0.029 statistically significant.

P value for Group II was 0.103 statistically not significant.

There was a statistically significant correlation noted between opportunistic infections and cardiac abnormalities in Group I ($P < 0.05$) in contrast to Group II ($P > 0.05$) which was insignificant.

ANALYSIS OF ELECTROCARDIOGRAM:

Out of 150 patients 22 patients had ECG abnormalities.

Table 23

ECG Abnormalities	CD4 Group I	CD4 Group II	TOTAL
Sinus tachycardia	1 (4.54%)	1 (4.54%)	2 (9.09%)
Conduction abnormalities	-	2 (RBBB) (9.09%)	2 (9.09%)
Atrial ectopic	1 (4.54%)	2 (9.09%)	3 (13.64%)
Ventricular ectopic	2 (9.09%)	-	2 (9.09%)
Poor progression of R wave	3 (13.64%)	1 (4.54%)	4 (18.18%)
Low voltage	5 (22.73%)	1 (4.54%)	6 (27.27%)
ST/ T wave abnormality	2 (9.09%)	1 (4.54%)	3 (13.64%)
Total	14 (63.64%)	8 (36.36%)	22 (100%)

ELECTROCARDIOGRAPHIC CHANGES IN RELATION TO CD4 COUNT

Table 24

ELECTROCARDIOGRAPHY	CD4 GROUP I	CD4 GROUP II	TOTAL
NORMAL	37 (24.7%)	91 (60.7%)	128 (85.3%)
ABNORMAL	14 (9.3%)	8 (5.3%)	22 (14.7%)
TOTAL	51 (34%)	99 (66%)	150 (100%)

P value was 0.000 statistically significant.

There was statistically significant difference noted between two groups regarding electrocardiographic abnormalities ($P < 0.05$) .

Prevalence of electrocardiographic abnormalities increased with decline in CD4 count.

ECHOCARDIOGRAPHIC FINDINGS:

Table 25

Sixteen of the 150 patients had ECHO abnormalities.

ECHOCARDIOGRAPHY	CD4 GROUP I	CD4 GROUP II	TOTAL
Pericardial Effusion	7 (43.75%)	2 (12.5%)	9 (56.25%)
Dilated Cardiomyopathy	4 (25%)	1 (6.25%)	5 (31.25%)
Septal Hypokinesia	1 (6.25%)	0 (0%)	1 (6.25%)
Infective Endocarditis	1 (6.25%)	0 (0%)	1 (6.25%)
Total	13 (81.25%)	3 (18.75%)	16 (100%)

ECHOCARDIOGRAPHIC CHANGES IN RELATION TO CD4 COUNT

Table 26

ECHOCARDIOGRAPHY	CD4 GROUP I	CD4 GROUP II	TOTAL
NORMAL	38 (25.3%)	96 (64%)	134 (89.3%)
ABNORMAL	13 (8.7%)	3 (2%)	16 (10.7%)
TOTAL	51 (34%)	99 (66%)	150 (100%)

P value was 0.000 statistically significant.

There was a statistically significant difference noted between two groups regarding echocardiographic abnormalities ($P < 0.05$).Prevalence of echocardiographic abnormalities increased with decline in CD4 count.

DISCUSSION

Cardiovascular manifestations of HIV infection have not attracted much attention in the Indian sub continent. This is partly because of the clinical picture of HIV infection still dominated by opportunistic infections and symptoms of breathlessness, fatigue and poor exercise intolerance are frequently ascribed to other conditions associated with HIV infection. With the greater access to Anti-retroviral medications more patients may live longer enough to present with end organ disorders. Our study throws light into various unsuspected cardiac abnormalities in various groups of HIV infected patients and its relationship to CD4 count.

A study conducted by Kannagai et al[57] at CMC Vellore in 2008 has shown that majority of the HIV infected individuals in South India with CD4 counts of 200 - 350 cells / mm^3 had higher viral load than that suggested by International AIDS Society.

Present study was undertaken based on the above observation. There are no supportive studies showing the comparison of prevalence of cardiac abnormalities with the CD4 counts of $\leq$ 350 cells/ mm^3 and $>$ 350 cells / mm^3.

AGE DISTRIBUTION

Our study population consisted of 150 patients. The mean age of our study group was 30.87 ± 6.11 years with the age group ranging from 22 to 50 years. Mean age of Group I and group II were 31.43 ±6.23 years and 30.58 ± 6.06 years respectively. In a study conducted by Joshi et al at Mumbai,[59] the age group ranged from 17 to 52 years with the mean age of 29.8 years.

Correlation between age, CD4 count and cardiac abnormalities was attempted. In Group I, out of 16 patients with cardiac abnormalities 3 patients were in 20 - 25 years age group, 4 patients were 26 - 30 years age group, 6 patients were in 31 - 35 years age group, one patient was in 36 - 40 years age group and 2 patients were in more than 40 years of age group. In Group II, out of 9 patients with cardiac abnormalities 3 patients were in 20 - 25 years age group, 4 patients were in 26 - 30 years age group, one patient each in 31 - 35 years and 36 - 40 years of age group. P values for Group I and Group II were 0.352 and 0.639 respectively which was statistically insignificant. There was no correlation between age and cardiac abnormalities in this study similar to the study conducted by Caggese et al.[60]

GENDER DISTRIBUTION

The gender distribution demonstrated a majority of 58.7 % (88) of females compared to 41.3% (62) of males. In a study conducted by Joshi et al [59], male and female ratio was 5.7:1 (63 males and 11 females). In P Kannan et al [61] study males were 120 and females were 80. In El Hattoui et al [62] study males and females were 88 and 70 respectively.

Sex distribution in relation to cardiac abnormalities and CD4 count was seen. In Group I, 9 males and 7 females had cardiac abnormalities. In Group II, 5 males and 4 females had cardiac abnormalities. P values for Group I and Group II were 0.801 and 0.118 respectively which was statistically insignificant. So sex did not play a significant role in cardiac abnormalities in HIV patients.

OCCUPATION

In our study group, house wives and unskilled labourers constituted majority of the population about 35% and 34.9% respectively. Skilled labourers were 6.67%, 18% was lorry driver, 2.7% was office workers and 1.3% was commercial sex worker and business man each.

ROUTE OF TRANSMISSION

Most of the study population had heterosexual behaviour (95.3%). Remaining were homosexual (0.7%), bisexual (0.7%), IV drug users (1.3%), blood transfusion related (1.3%) and unknown mode of transmission was 0.7%. In a study by Joshi et al, [59] among 74 patients 58.1% were heterosexuals, 4.05% blood transfusion related, 2.7% IV drug users, 1.35% bisexuals and 20.27% had multiple risk factors.

WHO STAGING

In our study, 50% of patients were in stage 1. Of the remaining 28% were in stage 2, 20% in stage 3 and 2% in stage 4. In Group I out of 16 patients with cardiac abnormalities, 3 patients were in stage 1, 3 patients were in stage 2, 7 patients were in stage 3 and 3 patients were in stage 4. P value was 0.024, statistically significant. In Group II, among 9 patients with cardiac abnormalities, 4 patients were in stage 1, 2 patients were in stage 2, 3 patients were in stage 3. P value was 0.169, statistically insignificant.

RISK FACTORS

In our study group, 7.3% were smokers and 8% were alcoholic. In Group I, 7.8% were smokers. Among 16 patients with cardiac abnormalities two patients were smokers. In Group II 7.1% were smokers.

All patients with cardiac abnormalities were non smokers. P values for both the groups were 0.403 and 0.385 respectively, statistically insignificant.

In Group I, 13.7% were alcoholics. Among 16 patients with cardiac abnormalities 3 were alcoholics. In Group II 5.1% were alcoholics. All patients with cardiac abnormalities were non alcoholics. P values for both the groups were 0.481 and 0.468, statistically insignificant. In a study by Smith CJ et al, [63] among 394 patients 45% were smokers and 7% were alcoholics. There was no significant correlation between smoking and alcohol with cardiac abnormalities in our study. This finding correlated well with the study by Caggese et al.[60]

DURATION OF HIV INFECTION

In this study 66% (99/150) of patients had duration of illness between 1 - 3 years. 12.7% (19/150) had less than a year and 21.3% (32/150) had duration of > 3 years. The duration of illness ranged from 3 months to 9.5 years. Mean duration of illness in study population (150 patients) was 3.18 years. Mean duration of illness in Group I and Group II were 2.95 years and 3.3 years respectively. In a study by P Kannan et al, [61] the duration of illness ranged from 6 months to 7 years.

In Group I, among 16 patients with cardiac abnormalities, 9 patients had a duration of > 3 years, 4 patients had a duration of 1 - 3 years and 3 patients had a duration of less than a year. P value was 0.00015, statistically significant. In Group II, among 9 patients with cardiac abnormalities 7 patients had a duration of > 3 years, 1 patient had a duration of 1 -3 years and 1 patient had a duration of less than a year. P value was 0.000, statistically significant. There was a significant correlation between duration of HIV infection and cardiac abnormalities.

SYMPTOMS

Most patients were asymptomatic. Only 10 (16.7%) patients had cardiac symptoms (Group I - 9, Group II - 1). Among 25 patients with cardiac abnormalities 40% (10 / 25) had symptoms. The symptoms were dyspnea (10.7%), fatigue (3%), palpitation (1.3%) and chest pain (0.7%). A significant correlation was found between cardiac abnormalities and cardiac symptoms. P values for both the groups were 0.000 and 0.001 respectively. In a study by Cardosa JS et al, [64] 7.3% (10 / 137) of patients were symptomatic. In a study by Ewig S et al, [65] nine out of 14 patients (64%) with cardiac abnormalities had symptoms.

BMI

The mean BMI of our study group was 20.40 ± 3.89 kg / m^2.

The mean BMI of Group I and Group II were 19.85 ± 4.01 kg / m^2 and 20.68 ± 3.82 kg / m^2 respectively.

In Group I, out of 16 patients with cardiac abnormalities, 7 were underweight, 2 patients were overweight and 7 patients had normal BMI. In Group II, out of 9 patients with cardiac abnormalities, 6 patients had normal BMI, one patient was underweight, one patient was overweight and one patient was obese. P values for Group I and Group II were 0.684 and 0.234 respectively, statistically insignificant. There was no significant correlation between BMI and cardiac abnormalities.

OPPORTUNISTIC INFECTIONS

In our study 23 patients (15.4%) had opportunistic infections. Oral candidiasis was the most common (8.7%) followed by tuberculosis (4%) and herpes zoster (2.7%). In Group I, out of 16 patients with cardiac abnormalities, 8 patients had opportunistic infections. P value was 0.029, statistically significant. In Group II, out of 9 patients with cardiac abnormalities, 2 patients had opportunistic infections. P value was 0.103, statistically insignificant. So fall in CD4 count proportionally increases the predisposition to both opportunistic infections and cardiac abnormalities.

In a study by De castro et al,[66] 72 patients (63%) had opportunistic infections or secondary malignancies. 45.6% had cardiac involvement presumably due to opportunistic infections and secondary malignancy. In Caggese L et al [60] study, no correlation was found between opportunistic infections and cardiac abnormalities.

ELECTROCARDIOGRAPHIC ABNORMALITIES

Electrocardiographic abnormalities were seen in 22 patients (14.7%). Nine Patients had ECG abnormalities without echocardiographic abnormalities. Three patients had normal ECG inspite of echocardiographic abnormality. In Group I, among 51 patients, 14 patients had ECG abnormalities. In Group II, 8 patients had ECG abnormalities. The ECG abnormalities observed were low voltage complexes (27.27%), poor progression of R wave (18.18%), non specific ST-T changes (13.64%), atrial ectopic (13.64%), right bundle branch block (9.09%), sinus tachycardia (9.09%) and ventricular ectopic (9.09%).There was a significant correlation between CD4 count and ECG abnormalities (P value was 0.000). In a study by Herdy GV et al, [67] out of 50 patients 18 patients had sinus tachycardia, 10 patients had ST-T changes, 5 patients had low voltage complexes, 5 patients had ST segment elevation and 3 patients had extra systole. In Mirri A et al [68] study, ECG abnormalities unrelated to echocardiographic abnormalities or clinical problems were

seen in 11 patients. In Joshi et al [59] study, among 74 patients, 20.27% had ECG abnormalities.

ECHOCARDIOGRAPHIC ABNORMALITIES

Prevalence of cardiac abnormalities by echocardiography in our study was 10.7% (8.7% in Group I and 2% in Group II). Echocardiographic findings were pericardial effusion (56.25%), dilated cardiomyopathy (31.25%), interventricular septal hypokinesia (6.25%) and infective endocarditis (6.25%). Group I revealed 81.25% (13/16) cases and Group II revealed 18.75% (3/16) cases with echocardiographic abnormalities. P value was 0.000, statistically significant. There was a significant correlation CD4 count and echocardiographic abnormalities. In a study by Joshi et al,[59] among 74 patients 10.6% had dilated cardiomyopathy, 8.5% had pericardial effusion, 4.2% had vegetations, 2.1% had constrictive pericarditis and 10.6% had incidental valvular, left ventricular hypertrophy, ischemic heart disease. In a study by Mishra et al [69] at AIIMS, 36.7% had diastolic dysfunction and 23.3% had systolic dysfunction. In P Kannan et al [61] study, out of 200 patients, 28 patients had left ventricular dysfunction, 20 patients had pericardial effusion, 6 patients had pulmonary hypertension and one patient had dilated cardiomyopathy. In Mirri A et al [68] study, 17% had echocardiographic abnormalities.

CARDIAC ABNORMALITIES

In our study among 150 patients, 25 patients (16.7%) had cardiac abnormalities either in the form of ECG or Echocardiography abnormality. It is observed that 16 patients out of 51 patients (31.4%) in Group I and 9 patients out of 99 (9.09%) patients in Group II had cardiac abnormalities. There was a statistically significant correlation between cardiac abnormalities and CD4 count (P value was 0.0001). As the CD4 count decreases, the cardiac abnormalities increase proportionally. Cardiac abnormalities are inversely proportional to CD4 count. This finding correlated well with Cardoso JS et al [65] study and Caggese et al [60] study. In a study by S Mishra et al [69], there was no correlation between CD4 count and diastolic dysfunction.

SUMMARY

The present study aimed at estimating the prevalence of cardiac abnormalities in HIV seropositive patients and also to find out its correlation with CD4 counts. With rigid criteria 150 HIV seropositive cases were selected. There were 62 males and 88 females in the study group.

Prevalence of cardiac abnormalities was 16.7% in our study.

Pericardial effusion was the most common echocardiographic abnormality.

Low voltage complex was the most common electrocardiographic abnormality.

Cardiac abnormalities were specifically correlated with CD4 counts. In this study 16 out of 51 patients with CD4 counts $\leq 350/mm^3$ had cardiac abnormalities. 9 out of 99 patients with CD4 counts of $> 350/mm^3$ had cardiac abnormalities.

Present study recommends screening for cardiac abnormalities in HIV patients to identify early cardiac involvement and minimize cardiac complications by early intervention.

CONCLUSION

1. The determination of Incidence and Prevalence of cardiac abnormalities in HIV infected individuals using non invasive tests is quite feasible and should be done in all patients registering in ART centre.

2. There was an inverse correlation between CD4 count and cardiac abnormalities. Decline in CD4count below 350 cells / mm^3 was associated with increased incidence of cardiac abnormalities.

3. There was a significant correlation between duration of HIV infection and cardiac abnormalities. Prevalence of cardiac abnormalities was found to be more with increase in the duration of HIV infection.

4. Most of the patients were asymptomatic. A significant correlation was found between cardiac symptoms and cardiac abnormalities.

5. Heterosexual route was the most common route of transmission of HIV.

6. Oral candidiasis was the most common opportunistic infection. There was a significant correlation between opportunistic infections and cardiac abnormalities.

7. There was no significant correlation between age, sex, BMI, smoking and alcohol with cardiac abnormalities**.**

LIMITATIONS

1. The mean duration of the disease in our patients was less. This could be responsible for decreased incidence of cardiac abnormalities in our patients.

2. Follow up study was not done. So the incidence of cardiac abnormalities in patients with previous normal echocardiography as well as the natural history of those who had Cardiac abnormality could not be studied.

3. Since the critically ill patients were not included in our study the entire spectrum of cardiac abnormalities could not be established.

5. Viral load could not be estimated due to constraints.

6. Histopathologic studies like pericardial biopsy, endomyocardial biopsy and cytological study of pericardial fluid to determine the etiology of pericardial effusion and cardiomyopathy were not done.

RECOMMENDATIONS

1. A baseline Echocardiographic study for all patients with HIV infection at first visit to be done.

2. Echocardiographic follow up should be done to determine the evaluation of cardiac abnormalities and their reversibility with or without treatment.

3. Histopathologic studies like pericardial biopsy, endomyocardial biopsy and cytological study of pericardial fluid to be done to determine the etiology of pericardial effusion and cardiomyopathy.

4. Autopsy studies should be performed in patients dying of HIV associated illness and this will throw light on exact incidence of cardiac abnormalities in HIV infected patients.

ABBREVIATION

AIDS	- Acquired Immuno Deficiency Syndrome
ANC	- Antenatal clinic
ART	- Anti Retro Viral Therapy
ATT	- Anti Tuberculous Therapy
BMI	- Body Mass Index
CD	- Cluster Differentiation
CNS	- Central Nervous System
CVS	- Cardiovascular system
DM	- Diabetes Mellitus
DNA	- Deoxyribonucleic acid
ECG	- Electrocardiography
Echo	- Echocardiography
FSW	- Female Sex Worker
HAART	- Highly Active Anti Retro Viral Therapy
HIV	- Human Immunodeficiency Virus
HT	- Hypertension
IDU	- Intravenous Drug Users
JVP	- Jugular venous pressure
LV	- Left Ventricle
MSM	- Men having sex with men
NACO	- National AIDS Control Organization
NACP	- National AIDS Control Programme

NHL	- Non Hodgkin’s Lymphoma
OH	- Orthostatic Hypotension
RNA	- Ribonucleic acid
RS	- Respiratory system
STD	- Sexually Transmitted Disease
WHO	- World Health Organization
Kg	- Kilo gram
µL	- Micro Litre
mm^3	- Cubic millimetre
m^2	- Metre square
>	- More than
≥	- More than or Equal
≤	- Less than or Equal
<	- Less than
%	- Percentage
±	- Plus or minus
&	- And

BIBLIOGRAPHY

1. Antony S.Fauci, H.Clifford Lane. Human Immunodeficiency Virus disease: AIDS and Related Disorders. Harrison's Principles Of Internal Medicine 17th edition, 2008: 1137-1204.

2. Ghosh TK; “AIDS: a serious challenge to public health”, Journal of the Indian Medical asociation,1986; 84(1): 29-30

3. UNAIDS 2008: Report on the global AIDS epidemic 2008, August 2008 (http://www.unaids.org)

4. Robert Steinbrook, M.D. HIV in India – A Downsized Epidemic. N Eng J Med 2008;358:107-109.

5. NACO.COM. HIV surveillance fact sheets and district categorization

6. NACO.COM. NACP III – criteria for ART.

7. WHO.com. Clinical staging of HIV and Antiretroviral Therapy Guidelines for HIV-infected adults and adolescents including Post-exposure Prophylaxis.

8. William Lewis / Peter F.Currie. HIV / AIDS and the Cardiovascular System. Hurst's The Heart, 12th edition chapter 92, 2118-2131.

9. Currie PF, Jacob AJ, Foreman AR et al. Heart muscle disease related to HIV infection: prognostic implications. Br Med J 1994;309:1605-1607.

10. Ntsekhe M, Hakim J. Impact of human immunodeficiency virus infection on cardiovascular disease in Africa. Circulation 2005;112:3947-3957

11. Pollock BH, Jenson HB, Leach CT, et al. Risk factors for paediatric human immunodeficiency virus-related malignancy. JAMA 2003;289:2393-2399.

12. Harmon WG, Dadlani GH, Fisher SD, Lipshultz SE: Myocardial and pericardial disease in HIV. Current Treatment Options cadiovasclar Med 4:497,2002.

13. Lipshultz SE, Fisher SD, Lai WW, Miller TL: Cardiovascular risk factors, monitoring and therapy for HIV-infected patients. AIDS 17:S96,2003.

14. Stacy D. Fisher and Steven E. Lipshultz. Cardiovascular Abnormalities in HIV-Infected individuals: Braunwald's Heart Disease 8th edition, chapter 67, 1793-1804.

15. Lewis W. Cardiomyopathy in AIDS. A pathophysiological perspective. Prog Cardiovasc Dis 2000;43:151-170

16. Levy WS, Simon GL, Rios JC, et al. Prevalence of cardiac abnormalities in human immunodeficiency virus infection. Am J Cardiol 1989;63:86-89.

17. Pugliese A, Isnardi D, Saini A, et al. Impact of highly active antiretroviral therapy in HIV-positive patients with cardiac involvement. J Infect 2000;10:405-412.

18. Rodriguez ER, Nasim S, Hsia J, et al. Cardiac myocytes and dentritic cells harbour human immunodeficiency virus in infected patients with or without cardiac dysfunction. Am J Cardiol 1991;68:1511-1520.

19. Herskowitz A, Willoughby S, Wu TC, et al. Immunopathogenesis of HIV-1 associated cardiomyopathy. Clin Immunol Immunopatho 1993;68:1511-1520.

20. Andrade LO, Machado CR, Chiari E, et al. Trypanozoma cruzi: role of host genetic background in the differential tissue distribution of parasite clonal populations. Exp parasitol 2002;100:269-275.

21. Ho DD, Pomerantz RJ, Kaplan JC. Pathogenesis of infection with human immunodeficiency virus. N Engl J Med 1987;317:278-286.

22. Kan H, Xie Z, Finkel MS. HIV gp120 enhances NO production by cardiac myocytes through p38 MAP kinase-mediated NF-B activation. Am J Physiol Heart Circ 2000;279:H3138-143.

23. Herskowitz A, Vlahov D, Willoughby S, et al. Prevalence and incidence of left ventricular dysfunction in patients human immunodeficiency virus infection. Am J Cadiol 1993;71:955-958.

24. Del prete G, Maggi E, Pizzlo G, et al. CD30 Th2 cytokines and HIV infection: a complex and fascinating link. Immunol Today 1995;16:76-80.

25. De Larranaga GF, Forastiero RR, Carreras LO, et al. Different types of antiphospholipid antibodies in AIDS. A comparison with syphilis and the antiphospholipid syndrome. Thromb Res 1999;96:19-25.

26. Brinkman K, Smeitnik JA, Romijn JA, et al. Mitochondrial toxicity induced by nucleoside-analogue reverse- transcriptase inhibitors is a key factor in the pathogenesis of antiretroviral-therapy-related lipodystrophy [comment] Lancet 1999;354:1112-1115.

27. Karch SB, Billingham ME, The pathology and etiology of cocaine induced heart disease. Arch Pathol Lab Med 1988;112:225-230.

28. Fuchs J, Ochsendrof F, Schofer H, et al. Oxidative imbalance in HIV infected patients. Med Hypotheses 1991;36:60-64.

29. Dworkin BM, Antonecchia PP, Smith F, et al. Reduced cardiac selenium content in the acquired immunodeficiency syndrome [see comments]. JPEN J Parenter Enteral Nutr 1989;13:644-647.

30. De simone C, Tzantzoglou S, Jirillo E, et al. L-carnitine deficiency in AIDS patients. AIDS 1992;6:203-205.

31. Moorthy LN, Lipshultz SE. Cardiovascular monitoring of HIV-infected patients. In: Lipshultz SE, eds. Cardiology in AIDS. New York: Chapman & Hall 1999;73:345-384.

32. Werneck GL, Mesquita ET, Romeo LJ, et al. Doppler echocardiographic evaluation of HIV-positive patients in different stages of the disease. Arq Bras Cardiol 1999;73:163-168.

33. Coudray N, de Zuttere D, Force G, et al. Left ventricular diastolic dysfunction in asymptomatic and symptomatic human immunodeficiency virus carriers: an echocardiographic study. Eur Heart J 1995;16:61-67.

34. Currie PF, Boon AB. Prospective adult cardiovascular morbidity and mortality studies: the world. In Lipshultz SE, eds. Cardiology in AIDS. New York: Chapman & Hall;1998:59-76.

35. Deswal A, Misra A, Bozkurt B. The role of anti-cytokine therapy in the failing heart. Heart fail Rev 2001;6:143-151.

36. Sliwa K, Woodiwiss A, Candy G, et al. Effects of pentoxifylline on cytokine profiles and left ventricular performance in patients with decompensated congestive heart failure secondary to idiopathic dilated cardiomyopathy. Am J Cardiol 2002;90:1118-1122.

37. Lipshultz SE, Orav EJ, Sanders SP, Colan SD: immunoglobulin and left ventricular structure and function in pediatric HIV infection. Circulation 1995;92:2220.

38. Brucato A, Colombo T, Bonacina E, et al. Fulminant myocarditis during HIV seroconversion: recovery with temporary left ventricular mechanical assistance. Ital Heart 2004;5:228-231.

39. Calabrase LH, Albrecht M, Young J, et al. Successful cardiac transplantation in an HIV-infected patient with advanced disease. N Eng J Med 2003;348:2323-2328.

40. Cammaraosano C, Lewis W. Cardiac lesions in acquired immunodeficiency syndrome (AIDS). J Am Coll Cardiol 1985;5:703-706.

41. Nahass RG, Weinstein MP, Bartels J, Infective endocarditis in intravenous drug users: a comparison of human immunodeficiency virus type-1 negative and positive patients. J Infect Dis 1990;162:967-970.

42. Harrison M, Tomlinson D, Stewart S. Liposomal entrapped doxorubicin: an active agent in AIDS-related Kaposi's sarcoma. J Clin Oncol 1995;13:914-920.

43. Saidi A, Bricker JT: Pulmonary hypertension in patients infected with HIV. In Lipshultz SE (ed): Cardiology in AIDS. New York, Chapman & Hall,1988;255-263.

44. Morse CG, Kovacs JA, Metabolic and skeletal complications of HIV infection: The price of success. JAMA, 2006; 296:844.

45. Schecter AD, Berman AB, Yi L, et al. HIV envelope gp120 activates human arterial smooth muscles. Proc Natl Acad Sci USA 2001:98:10142-10147.

46. Kanmogne GD, Primeaux C, Grammas P. Induction of apoptosis and endothelin-1 secretion in primary human lung endothelial cells by HIV-1 gp120 proteins. Biochem Biophys Res Commun 2005;333:1107-1115.

47. Recusani F, Di Matteo A, Gambarin F, et al. Clinical and therapeutical follow-up of HIV-associated pulmonary hypertension: prospective study of 10 patients. AIDS 2003;17(suppl 1):S88-95.

48. Pugliese A, Gennero L, Vidotto V, et al. A review of cardiovascular complications accompanying AIDS. Cell Biochem Funct 2004;22:137-141.

49. Cea-Calvo L, Escribano Subias P, Tello de Menessess R, et al. Treatment of HIV-associated pulmonary hypertension with treprostinil. Rev Esp Cardiol 2003;56:421-425..

50. Ene L, Goetghebuer T, Hainaut M, et al. Prevalence of lipodystrophy in HIV-infected children: A cross sectional study. Eur J pediatr 2007;166:13.

51. Grinspoon S, Carr A: Cardiovascular risk and body fat abnormalities in HIV- infected adults. N Eng J Med 2005;352:48.

52. Fisher SD, Miller TL, Lipshultz SE: impact of HIV and HAART on Leukocyte adhesion molecules, arterial inflammation, dyslipidemia and atherosclerosis. Atherosclerosis 2006;185:1.

53. Hadigan C, Meigs JB, Wilson PW, et al.prediction of coronary heart disease risk in HIV-infected patients with fat redistribution. Clin Infec Dis 2003;36:909.

54. Correia D, Rodrigues De Resende LA, Molina RJ, et al. Power spectral analysis of heart rate variability in HIV-infected and AIDS patients. Pacing Clin Electrophysiol 2006;97:1657.

55. Sani MU, Okeahialam BN, Qtc interval prolongation in patients with HIV and AIDS. J Natl Med Assoc 2005;97:157.

56. Nordin C, Kohli A, Beca S, et al. Importance of hepatitis C co infection in the development of QT prolongation in HIV-infected patients. J Electrocardiol 2006;185:1.

57. R Kannangai, AJ Kandathil, DL Ebenezer, G Nithyanandam, P Samuel, OC Abraham, TD Sudarsanam, SA Pulimood, G Sridharan. Evidence for lower $CD4^+$ T cell and higher viral load in asymptomatic HIV-1 infected individuals of India: Implications for therapy initiation. Indian Journal of Medical Microbiology, (2008) 26(3): 217-221.

58. Appropriate BMI for Asian population and its implications for policy and intervention strategies. WHO expert consultation. Lancet 2004;363:157-163.

59. Joshi S, Deshpande AK, et al. Cardiac involvement in Indian HIV population. Int Conf AIDS 1998;12:575 (abstract no. 32278).

60. Caggese L, Mantero A, Schlacht I, Orcese C, et al. Cardiac involvement in HIV infection. Int Conf AIDS.1991 Jun 16-21;7(1):283 (abstract no. M.B.2404).b

61. P Kannan, RA Janarthanan, S Palanichamy,et al. **C**ardiovascular Manifestations in HIV Infected Patients. Indian Heart Journal Sep–Oct, 2003; 55:(5) Article no. 538 .

62. El Hattaoui M, Charei N, Boumzebra D, et al. Prevalence of cardiomyopathy in HIV infection.. Med Mal Infect 2008 Jul;38(7):387-91. Epub 2008 jun 25.

63. Smith CJ, Levy I, Sabin CA, Kaya E, et al. Cardiovascular risk factors and antiretroviral therapy in an HIV positive UK population. HIV med 2004 Mar;5(2):88-92.

64. Cardosa JS, Miranda AM, Moura B, Gomes MH, et al. Cardiac morbidity in the human immunodeficiency virus infection. Rev Port Cardiol 1994 Dec;13(12):901-11.

65. Ewig S, Fehske W, Omran H, Rockstroh JK, Luderitz B, et al. Cardiac manifestations in advanced HIV infection. Dtsch Med Wochenschr 1994 May 13;119(19):83-9.

66. De Castro S, Migliau G, Silvetri S, et al. Heart involvement in AIDS: a prospective study during various stages of the disease. Eur Heart J 1992 Nov;13(11):1452-9.

67. Herdy GV, Ramos R, Bazin AR, Herdy AH, et al. Clinicopathological correlation in 50 cases of acquired immunodeficiency syndrome. Retrospective study. Arq Bras Cardiol 1994 Feb;62(2):95-8.

68. Mirri A, Rapezzi C, Iacopi F, Ortolani P, et al. Cardiac involvement in HIV ivfection. A prospective, multicenter clinical and echocardiographic study. Cardiologica 1990 mar;35(3):203-9.

69. S Mishra, N Wig, CM Mittal, RM Pandey, G Karthikeyan, P Arora, VK Bahl et al. Diastolic Dysfunction in Human Immunodeficiency Virus (HIV)-Infected Patients in North India. Indian Heart Journal Sept-Oct, 2003; 55:(5) Article No. 166

70. Gazzard B, Bernard EJ, Boffito M, Churchill D, Edwards S, Fisher M, e al. BHIVA writing committee: British HIV Association (BHIVA) guidelines for the treatment of HIV-infected adults with antiretroviral therapy (2006). HIV Med 2006;7:487-503.

71. Hammer SM, Saag MS, Schechter M, Montaner JS, Schooley RT, Jacobson DM, et al. Treatment for adult HIV infection: Recommendations of the International AIDS society-USA panel. JAMA 2006;296:827-43.

72. Ramalingam S, Kannangai R, Zachariah A, Mathai D, Abraham C. CD4 counts of normal and HIV-infected south Indian adults: do we need a new staging system. Natl Med J India. 2001 Nov-Dec;14(6):335-9.

PROFORMA

Name	Hospital No:	Serial No:
Age		
Sex	Height	WHO Stage:
Occupation	Weight	Education :
Address	BMI	

Marital status

Sexual exposure

Other risk factors

Partners HIV status

Duration of HIV infection

Age at first sexual exposure

Recent extra marital exposure

Previous STD's

Present STD's

Smoking

Alcohol

DM

HT

Previous cardiac illness

H/O ATT

PRESENTING COMPLAINTS

Chest pain
Breathlessness
Palpitation
Pedal edema
Fatigue
Postural giddiness

EXAMINATION

Pallor
Jaundice
Cyanosis
Clubbing
Pedal edema
Lymphadenopathy

BP: Supine - Standing -
Pulse rate Respiratory Rate Temperature
JVP
Opportunistic infections

CVS
RS
ABDOMEN
CNS

INVESTIGATIONS

HEMOGRAM CD4 count -

Hb%
Total count
Differential count P - , L - ,E - ,M - ,B - .
ESR
PCV
Platelet count

RENAL FUNCTION TEST

Blood urea
Blood sugar
Serum creatinine
Serum electrolytes

LIPID PROFILE

Total Cholesterol
Triglycerides
HDL
LDL
VLDL

LIVER FUNCTION TEST

Serum Bilirubin
SGOT
SGPT
Sr. Alkaline Phosphatase
Total Protein
Albumin
Globulin

ECG

Chest X ray

Echocardiography